REMARKS

Claims 40-47 are pending and stand rejected. The claims are directed to peptides that represent portions of the STEAP-1 protein that are able to raise antibodies which are immunoreactive with the STEAP-1 protein. The Office has not questioned this ability, nor has the Office has questioned that the specification teaches how to make and use the antibodies raised. For example, page 20, lines 29-30 of the specification, specifically states that STEAP antibodies are useful in prostate cancer therapeutic strategies, diagnostic and prognostic assays. Page 21 of the specification is a reminder that methods to prepare antibodies are well known in the art and some discussion of what these art-known ways are, is set forth there. Page 22 of the specification sets forth three of the four peptides recited in claim 40 as being particularly useful, and the fourth peptide is exemplified in a working example. Known ways to humanize antibodies, etc. are also referred to in the specification. As set forth on page 27, STEAP-1 protein is expressed at high levels in several human cancers, including prostate, bladder, colon and ovarian and Ewing carcinoma. As noted, the STEAP-1 protein in normal tissue is largely restricted to the prostate. Page 28, lines 18-20 of the specification, states that since STEAP-1 is uniformly expressed at high levels over the surface of prostate glandular epithelia, immunotherapeutic intervention strategies that target extracellular STEAP epitopes are possible. Cancer immunotherapy using anti-STEAP antibodies is specifically set forth on page 29, lines 23-31 of the specification, where it is clearly stated that methods of conducting such therapy are known in the art. The referred-to sections are merely exemplary of the guidance provided throughout the specification that the antibodies raised with respect to the claimed peptides are useful both for diagnosis and therapy of the specified tumors.

Applicants understand that the Office does not question that the application is enabling regarding how to execute these uses of the invention, provided that the underlying natural behavior of STEAP-1 protein is such that application of these art-known methods with the novel antibodies raised using the claimed peptides provides a useful result. In order for that result to occur, the Office argues that applicants must:

1. demonstrate the absence of the STEAP-1 protein in normal tissue as compared to cancer tissue; or

2. demonstrate that STEAP-1 protein is present in patient cancer samples from tissues where STEAP-1 is normally absent.

With respect to the first item, it may be correct that the high levels of STEAP-1 in normal prostate make it difficult to utilize STEAP-1 protein levels as a marker for prostate cancer. However, the presence of STEAP-1 protein in normal prostate does not preclude the use of STEAP-1 antibodies for the immunotherapeutic treatment of prostate cancer. While normal prostate tissue is as vulnerable as the cancer tissue, perhaps, to treatment by these antibodies, this is of no consequence as the prostate is a disposable organ. There is nothing of record which would indicate that it is incredible to treat a cancer with antibodies to a tumor-associated antigen and the well-known examples of Herceptin® and Rituxan® are proof that this is the case.

Nevertheless, as discussed at the interview, applicants actually have data which demonstrate that antibodies raised against STEAP-1 would be useful in the treatment of prostate cancer. Enclosed herewith is the declaration of Dr. Jean M. Gudas, Ph.D., which authenticates the exhibits discussed at the interview. Applicants understand from the discussion that took place at the interview, that such authentication would be sufficient to verify the data in the exhibit, demonstrate

that the antibodies that so raised, were useful regarding prostate cancer treatment, diagnosis and prognosis. Applicants therefore believe that the submission of this declaration, in addition to the arguments set forth above, place the application in a position for allowance.

In summary, even though STEAP-1 protein is produced in normal prostate, this does not preclude the use anti-STEAP-1 antibodies to treat prostate cancer; indeed, the high levels of STEAP-1 in the prostate may actually be helpful to mediate effective treatment. And it may not even be necessary to test particular prostate cancers for the presence of STEAP-1, since as shown in Figure 5 and Figure 6 of the specification, all samples of prostate cancer tested express this protein.

In view of the foregoing declaration and exhibits, the following is essentially moot with regard to passing the application to issuance. However, for completeness, applicants wish to put on the record their view that the evidence already presented concerning the presence of STEAP-1 protein in various cancer cell lines is itself adequate to support utility for this protein.

The Office acknowledges that normal tissues other than prostate have essentially undetectable levels of STEAP-1 protein, but asserts that it is not sufficient to demonstrate that various cell lines derived from pancreatic, colon, bladder, EWS, breast, testicular, cervical, and ovarian cancer, as well as ALL, show high expression levels for this protein. The Office argues that as this has been shown only in cancer cell lines and this showing is insufficient proof that the protein will be present in actual cancer samples. In support, the Office quotes generalized statements that petri-dish cancer is poor representation of malignancy. The Office states that although protein may be produced by a cancer cell line, the corresponding human cancer may not produce this protein. The argument is based on the concept that the culture environment is different from the environment *in vivo*.

Applicants do not dispute that an *in vitro* cell culture environment differs from an *in vivo* one. Nevertheless, this does not mean that it necessarily follows that a protein expressed in a cultured cancer cell lines would not be expressed in the corresponding cancer *in vivo* or that the expression of the protein in the relevant cultured cell line is meaningless. There is no evidence of record showing that proteins highly expressed in a cancer cell line were not expressed in the cancer from which it was derived. In addition, absolute certainty is not required. A utility need only be specific, substantive, and credible. The production of STEAP-1 protein by the multiplicity of cell lines shown in Figures 5 and 6 clearly indicates to the skilled artisan that it is highly probable that this protein is expressed in at least some cancers of the corresponding organ. And, since these organs do not normally produce STEAP-1 protein, an assay for the presence of this protein as a prerequisite for treatment is practicable. This, again, mimics the pattern of Herceptin® where only those breast cancers that produce the HER2 protein are candidates for treatment with Herceptin®. This is a further reminder that not each and every cancer corresponding to the organ of origin of the cell line tested need produce this protein to make the antibodies of the invention useful.

Thus, in summary, in addition to the arguments above, applicants have presented a declaration, kindly acknowledged by the Examiner to be satisfactory to demonstrate that the antibodies generated by the claimed protein fragments are useful and that the specification meets the requirements of 35 U.S.C. § 112 in accordance with *In re Brana*, 34 USPQ2d 1436 (Fed. Cir. 1995). Accordingly, applicants believe that the pending claims, claims 40-47, are in a position for allowance and passage of these claims to issue is respectfully requested. If the Examiner believes that a telephone discussion would be helpful, a telephone call to the undersigned would be greatly

appreciated. Again, applicants wish to express their appreciation to the thoughtful consideration provided by the Examiner at the interview.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 511582001621.

Dated: May 3, 2004

Respectfully submitted,

By _____
James J. Mullen, III
Registration No.: 44,957
MORRISON & FOERSTER LLP
3811 Valley Centre Drive, Suite 500
San Diego, California 92130
(858) 720-7940